Bowditch (H. P.)

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AN

ADDRESS

BEFORE THE

BIOLOGICAL SECTION

OF

THE AMERICAN ASSOCIATION

FOR THE

ADVANCEMENT OF SCIENCE

AT THE

BUFFALO MEETING, AUGUST, 1886.

BY

H. P. BOWDITCH,

VICE-PRESIDENT, SECTION F.

[From the PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, Vol. XXXV.]

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With the compliments of

Dr. H. P. Bowditch.

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PROF. H. P. BOWDITCH,

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WHAT IS NERVE-FORCE?

Ever since I learned that the honor which had been conferred upon me of presiding over the section of biology involved the constitutional obligation of producing an opening address, I have been led to speculate upon the wisdom of the provision which compels a presiding officer thus to occupy the time of his section with formal remarks.

In the early days of the Association it may have been found desirable to stimulate the literary activity of the members, and to secure by a constitutional provision the presentation each year of a certain number of more or less carefully prepared papers; but now, when time can scarcely be found for the discussion of the really valuable papers awaiting consideration, a chairman would indeed show himself strangely insensible to the duties of his post who should, by perfunctory remarks of his own, long detain his section from the important work which has called them together.

I would not of course be understood as speaking disparagingly of the addresses of former vice presidents in this and other sections of the Association. It is doubtless true that many valuable contributions to science have found their way to the public through the medium of an annual address, but it may be fairly asked whether these same contributions would not have been made through some other channel if the writer had not found himself thus called upon to address his section.

A worker in the field of science who has a message which he

feels called upon to deliver to his brethren is sure to find some means of making himself heard ; nor can it be said that a volume of transactions, even of such an active association as our own, offers a particularly favorable medium for such a communication. In fact, the special journals of science, in the promptness of their appearance and the extent of their circulation, have such an advantage over the transactions of an association as channels for the conveyance of scientific thought, that it is not uncommon to hear the exaggerated opinion expressed that an article might as well not be printed at all as buried in a volume of transactions.

But whether volumes of transactions or special journals are the chosen medium of communication, it is clear that the literary activity of workers in science needs no stimulation at the present time. The constantly increasing difficulty which specialists, even in quite narrow fields, find in keeping themselves posted with regard to progress in their lines of work is a sufficient proof of the correctness of this statement.

The accumulated literature in every department of science is already so enormous in amount and is increasing at such a rapid rate that any association or individual undertaking to contribute thereto should do so only under a sense of grave moral responsibility.

Under these circumstances is it not desirable for the members of this Association to consider whether the best interests of science would not be served by so amending the article of the constitution, which requires annual addresses by the vice presidents, as to make it permissive and not mandatory in its provisions?

Having thus entered my protest against a system which places me before you in the position of one who has got to say something rather than of one who has got something to say, I will proceed to comply with the regulation and will ask your attention for a few moments to some of the evidence which has been recently collected relating to one of the most important problems of physiology. A distinguished biologist has remarked with great truth that the study of the nervous system is the true field of battle for physiologists, all other investigations, however interesting and important, being of the nature of skirmishes, preparatory for and leading up to the final conflict in which we must engage before we can hope to gain a position from which nature's most mysterious processes are laid bare to our view. Of all the functions of the nervous system,

the one which at first sight would seem most accessible to investigation is that of the nerve fibre itself. What conception can we form of the physical or chemical changes which take place in those white glistening bands which are for us the only channels through which knowledge of the physical universe can be obtained and which also enable us to impress upon the world around us the evidence of our conscious personality?

From the earliest times this problem has been earnestly discussed by physiologists but I do not intend to weary you with an account of the various crude theories which have been from time to time advanced. With the discoveries of Du Bois Reymond, the hope arose that nerve activity might be explained as an electrical phenomenon and the attempts made to build up a satisfactory electrical theory of nervous action have been numerous and ingenious. The important facts which forbid the identification of nerve force with electricity are the absence of an insulating sheath on the nerve fibre, the slow rate at which the nerve force is transmitted, and the effect of a ligature on a nerve in preventing the passage of nerve force while not interfering with that of electricity. The electrical phenomena connected with the functional activity of nerves (action current, electrotonus) appear, therefore, to be secondary in their character and not to constitute the essential process in nerve action. In this connection should be noted an experiment of d'Arsonval[1] which shows how the electrical phenomena associated with the activity of nerves may be imitated by purely physical means. This observer filled a glass tube of one or two millimeters interior diameter with drops of mercury alternating with drops of acidulated water, thus forming a series of capillary electrometers. The tube was closed at its two ends with rubber membranes and was provided with lateral openings by which its interior could be connected with electrical conductors. A blow upon one of the membranes caused an undulation of the liquid column which was propagated from one end to the other of the tube and was accompanied by a wave of electrical oscillation which was propagated *at the same rate.* The phenomenon is, according to d'Arsonval, to be explained as follows: The blow upon the membrane changes the form of the surface of contact between the first two cylinders of mercury and acidulated water. This change of form is transmitted to the following cylinders with a rapidity dependent upon the na-

[1]Comptes rendus de la Soc. de Biologie, Apr. 3, 1886.

ture of the fluid. But each of these changes of shape is accompanied by the production of an electric current (Lippmann's phenomenon or variation of superficial tension) and the tube is therefore traversed by an electric wave which necessarily has the same rate as the undulation of the liquid column. The analogy between this phenomenon and the wave-like propagation of the action current in nerves is sufficiently obvious.

In studying the nature of nerve force two alternatives present themselves. We may conceive the impulse to be conducted through the nerve fibre by a series of retrograde chemical changes in the successive molecules of the nerve substance, the change occurring in one portion of the fibre acting to produce a similar change in the neighboring portion. As this process is associated with the using up of organic material and the consequent discharge of potential energy in the successive portions of the nerve, the theory may be called *the discharging hypothesis.* The burning of a line of gunpowder may be taken as an example of this sort of action.

On the other hand, we may conceive that the nerve force is transmitted from molecule to molecule by some sort of vibratory action as sound is transmitted through a stretched wire. As this theory does not involve the using up of any material but simply the transferring of motion, it may be called *the kinetic hypothesis.*

Let us now enquire what evidence can be obtained in favor of one or the other of these hypotheses by the study of the changes which are associated with the activity of nerves.

Inasmuch as the discharging hypothesis involves the destruction of organic material we may, if this theory be correct, reasonably expect to find in the active nerve fibre evidences of chemical decomposition and of heat production. Morever if the organic substances are used faster than they are replaced, or their products of decomposition removed, as would naturally be the case under constant stimulation, we may expect to observe a diminution of nerve action during the continuance of the stimulation: in other words we shall have the phenomena of fatigue.

On the kinetic hypothesis, on the other hand, we may expect to find an entire absence of chemical decomposition and fatigue and, if the moving particles are endowed with perfect elasticity, an absence also of heat production.

We must therefore consider what results have been reached by the experimental study of these three subjects, viz., the chemical

changes, the heat production and the fatigue of active nerve fibres, and ascertain whether these results are more favorable to a discharging or a kinetic theory of nerve action.

Chemical Changes.

The only functional chemical change of nerves for the existence of which an experimental proof has been offered is the change in the reaction to test paper. Just as the normally alkaline tissue of muscles becomes neutral or acid in activity, so, according to Funke[2] and Ranke[3], do nerve fibres and the white substance of the spinal cord change in activity from an alkaline to an acid reaction.

Liebreich[4] and Heidenhain[5], on the other hand, experimenting with a slightly different method, failed to get any evidence of the acidification of nerves in connection with functional activity.

Hermann, in the *résumé* of this subject given in his Handbook of Physiology (2, I, 139), gives his opinion that, while Funke's statement as to the irritative acidification of nerves has not been disproved, yet the phenomenon is of so delicate a nature that it can be detected only by the most sensitive reagents. The phenomenon must indeed be a delicate one since Ranke himself urges that the question should be decided by experiments on the spinal cord and should not depend upon the "doubtful results of tests applied to the nerve trunks." Now since the cord contains gray as well as white substance and as the gray substance, according to Ranke himself, becomes more acid than the white in functional activity it is clear that an acid reaction of the white substance of the spinal cord may depend upon an acid formed in the gray and passing by diffusion into the white substance. This possibility, which is indeed admitted by Ranke, seems to deprive the experiments on the spinal cord of what little value they possessed as evidence of the production of acid in connection with the activity of nerve fibres.

The other chemical changes which have occasionally been asserted to occur in active nerves rest on still weaker experimental evidence and it is therefore clear that chemical investigation gives us but little reason for maintaining a discharging in opposition to a kinetic theory of nerve action.

[2]Archiv. für Anat. und Physiologie, 1859, S. 835.
[3]Centralblatt f. d. med. Wiss. 1868, S. 769; 1869, S. 97.
[4]Tagebl. d. Naturf. Vers. zu Frankfurt 1867, S. 73.
[5]Studien IV, S. 248; Centralbl. f. d. med. Wiss. 1868, S. 833.

Heat Production.

The first experiments to test the heat production of active nerves were those of Helmholtz[6] who, after studying the analogous phenomenon in muscles, extended his investigations to nerve fibres. He failed, however, when all sources of error were carefully avoided, to obtain any evidence of heat production in connection with nervous activity, though his apparatus was capable of registering a change of temperature of 0.002° C.

Similar negative results were obtained by Heidenhain[7] who also experimented with the most delicate forms of thermo-electric apparatus.

On the other hand Valentin,[8] Oehl[9] and Schiff[10] maintain the affirmative side of the question, asserting that nerve fibres really are warmed by the passage of the nerve impulse. The statements of the latter observer are, however, rendered somewhat suspicious by the fact that he found the nerve fibre warmer at a point near than at one distant from the point irritated. This is explained by Schiff on the untenable hypothesis that the nerve impulse diminishes in intensity as it passes along the fibre.

In summing up the evidence on this question it is important to bear in mind that the methods of research employed by Helmholtz and Heidenhain were, to say the least, as accurate and as delicate as those of the other observers and we may, therefore, safely agree with Hermann (Handbook 2, I, 143) that the question whether a nerve produces heat on stimulation must be regarded as not yet settled, but if heat production does occur it must be exceedingly slight.

It seems, then, that the results of thermometric investigations speak no more positively than those of chemical research in favor of a discharging rather than a kinetic theory of nerve action.

Fatigue.

Without entering upon the question whether deficiency of decomposable organic material or accumulation of its products of decomposition is the essential chemical condition of fatigue, it will be sufficient for our purpose to consider what evidence there is that a nerve fibre, kept constantly stimulated, becomes less capable

[6] Archiv. für Anat. und Physiologie, 1848, S. 158.
[7] Studien IV, S. 250.
[8] Moleschott Undersuch. IX, S. 225.
[9] Gaz. Med. de Paris 1886, p. 225.
[10] Pflüger's Archiv, IV, S. 230.

of performing its function, *i. e.*, of transmitting the impulse to the organs with which it is connected.

The evidence of the activity of a nerve may be either direct or indirect. The direct evidence consists in the occurrence of that change of the electrical condition known as the "negative variation" of Du Bois Reymond or the "action current" of Hermann. The latter writer quotes the former as authority for the statement that this phenomenon becomes less intense in successive repetitions of the experiment and regards this as evidence of the exhaustion of the nerve fibre. Unfortunately Hermann does not refer to the exact passage which contains this statement and an examination of the chapter on the negative variation of nerves in Du Bois Reymond's Untersuchungen fails to show any systematic study of the effects of fatigue on this phenomenon. Indeed, the method employed by Du Bois Reymond seems poorly adapted for such a study and the diminishing intensity of the negative variation noticed by this observer[11] may very possibly have depended upon causes not connected with the exhaustion of the nerve by its functional activity.

The indirect evidence of the activity of a nerve consists in the effect which it produces upon the central and peripheral organs with which it is connected. Of these effects the contraction of a muscle is the one which is most conveniently observed, but the fact that a muscle is more readily exhausted than a nerve renders it impossible to study the fatigue of nerves in this way without some special modification of the experiment.

Bernstein[12] was the first to employ the mnscular contraction in experiments on the exhaustion of nerves. This observer applied a tetanic stimulation to the nerves of two nerve-muscle preparations through one of which, at a point on the nerve between the place stimulated and the muscle, a constant current of electricity was sent. The stimulus was thus prevented from reaching the muscle in one preparation while in the other its passage was unimpeded. While the latter muscle therefore was tetanically contracted, the former remained at rest. After the contracting muscle had become entirely exhausted, the constant current through the other preparation was opened and the muscle, which had been previously at rest, immediately contracted, thus

[11] Untersuchungen, II, 425. [12] Pflüger's Archiv, XV, 289.

showing that the nerve had not become exhausted by a stimulation which had lasted long enough to exhaust the muscle. To determine how long a stimulation was necessary in order to exhaust the nerve this method was not used because it was found that, after the prolonged passage of a constant current through the nerve, the opening of the current of itself caused a contraction (opening-tetanus) even without any stimulus applied above.

By a somewhat modified method, however, Bernstein reached the conclusion that a nerve may be exhausted by 5′–15′ tetanic stimulation.

The experiments of Bernstein have recently been repeated by Wedenskii[13] who, by using a feeble polarizing current and by frequently changing its direction, was able to avoid the opening tetanus which had led Bernstein to abandon this method of investigation. Experimenting in this way Wedenskii was unable to find any evidence of the exhaustion of the nerve even after the tetanic stimulation had continued six hours. The opening of the constant current was invariably followed by a muscular contraction, which was proved to be due to the tetanic stimulation applied above by the fact that, when this stimulation was omitted, the opening of the constant current had no effect.

Another method of stopping the passage of the stimulus through the nerve to the muscle is by poisoning the animal with curare. In the case of an animal poisoned by this drug, a continued stimulation of a nerve should remain without effect upon the muscle connected with it as long as the animal continues under the influence of the poison, but as soon as the drug is sufficiently eliminated the muscle should begin to twitch. The use of the drug for this purpose was suggested by Wedenskii, but his experiments, which were made on frogs, do not seem to have been successful.

Their failure may well be supposed to depend upon the slow and uncertain manner in which curare is eliminated by these animals, and a study of the subject upon warm-blooded animals seeming desirable, experiments were made upon cats in the laboratory of the Harvard Medical School.[14] The animals were kept under the influence of a dose of curare just strong enough to prevent muscular contractions, while artificial respiration was maintained

[13] Centralblatt für die med. Wissenschaften, 1884, p. 65.
[14] Bowditch, Journal of Physiology, VI, 133.

and the sciatic nerve constantly subjected to stimulation sufficiently intense to produce in unpoisoned animals a tetanic contraction of the muscles. In this way it was found that stimulation of the nerve lasting from $1\frac{1}{2}$ to 4 hours (the muscle being prevented from contracting by curare) did not exhaust the nerve, since on the elimination of the curare the muscle began to contract.

It thus appears that evidence of fatigue in nerves resulting from functional activity is as difficult to obtain as that of chemical change or of heat production. A nerve isolated from the body for experimental purposes will of course gradually lose its irritability; but this change, which was observed by Du Bois Reymond, as above mentioned, seems to be associated with the gradual death of the nerve due to its altered surroundings rather than to physiological fatigue. It is conceivable that the *irritability* of a nerve should depend upon its possessing a certain definite chemical composition constantly maintained by metabolic changes and yet that the *irritation* of the nerve should produce no change whatever in its composition.

In support of this view an analogy may be drawn from the physiology of the muscular system. We find here that the power of the muscles to perform their function is intimately associated with the amount of nitrogenous material undergoing decomposition in the body but the performance of a given amount of muscular work, if within physiological limits, does not affect the amount of nitrogen excreted. In the case of muscles, to be sure, we have evidence of a considerable decomposition of non-nitrogenous material and also of heat production in connection with functional activity, but, if we limit our consideration to the nitrogenous element of muscular substance, the hypothesis above proposed for nerves finds its complete analogy in the muscular system.

The connection between nerves and muscles is so close that the muscular fibre has been described as "the contractile termination of the nerve." If the hypothesis here suggested be correct, we have a possible explanation of this close connection, for we may conceive that the vibratory impulse, after traversing the nerve fibre, continues its course through the muscular substance, producing in the nitrogenous portion of the muscle-molecule a kinetic change similar to, or identical with, that which occurs in the nerve, and, at the same time, setting up in the adjacent non-nitrogenous

portion, an explosive decomposition, the result of which is manifested as a muscular contraction.

Without, however, indulging in further speculation, let it suffice for the present to note the fact that investigations into the chemical changes, the heat production and the fatigue of active nerves all lead to results more favorable to a kinetic than to a discharging theory of nerve action.

We may, therefore, reasonably hope that future researches, if directed on this line, will throw further light on this most mysterious and interesting process.